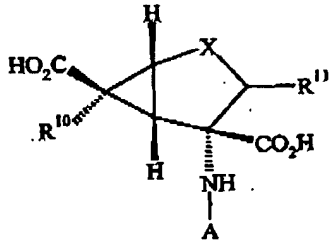
Amendments to the Claims

Please cancel Claims 1 through 37 submitted in the previous Preliminary Amendment on November 30, 2004. Please amend the claims as follows:

1-37. Cancelled.

38. (New): A compound of Formula I



(I)

wherein:

A is H-$(Q)_p$-;

Q is independently selected, each time taken, from the group amino acyl;

p is an integer from 1 to 10;

X is O, S, SO, SO_2, or CR^3R^4;

R^3 is fluoro, X'OR^5, SO_3H, tetrazol-5-yl, CN, $PO_3R^6{}_2$, hydroxy, NO_2, N_3, $(CH_2)_mCOOR^{5a}$, $(CH_2)_mPO_3R^{6a}{}_2$, $NHCONHR^{5b}$, or $NHSO_2R^{5c}$ and R^4 is hydrogen; or R^3 and R^4 each represent fluoro; or R^3 and R^4 together represent =O, =NOR^7, =CR^8R^9, =$CHCOOR^{5b}$, =$CHPO_3R^{6a}{}_2$, or =CHCN; or one of R^3 or R^4 represents amino and the other represents carboxyl;

X' represents a bond, CH_2, or CO;

m is an integer from 1 to 3;

R^5, R^{5a}, R^{5b}, R^{5c}, R^7, R^8, and R^9 are independently a hydrogen atom; an optionally substituted (1-6C) alkyl group; an optionally substituted (2-6C) alkenyl group; an optionally substituted (2-6C) alkynyl group; an optionally substituted aromatic group; an optionally substituted heteroaromatic group; a non-aromatic carbocyclic group; a non-aromatic heterocyclic group; a non-aromatic monocyclic carbocyclic group fused with one or two monocyclic aromatic

or heteroaromatic groups; or a non-aromatic monocyclic heterocyclic group fused with one or two monocyclic aromatic or heteroaromatic groups;

R^6 and R^{6a} independently represent hydrogen or a (1-6C)alkyl group;

R^{10} is hydrogen or fluoro; and

R^{11} is hydrogen, fluoro, or hydroxy;

or a pharmaceutically acceptable salt thereof.

39. (New): A compound or salt according to Claim 38, provided that the compound or salt is not one in which X is CR^3R^4 wherein R^3 is fluoro and R^4 is hydrogen, p is 1, and Q is L-alanyl; or a pharmaceutically acceptable salt thereof.

40. (New): A compound or salt according to Claim 38 wherein

A is $H-(Q)_p-$;

Q is independently selected, each time taken, from the group amino acyl;

p is an integer from 1 to 3;

X is O, S, SO, SO_2, or CR^3R^4;

R^3 is fluoro or hydroxy, and R^4 is hydrogen; or R^3 and R^4 together represent =O;

R^{10} is hydrogen or fluoro; and

R^{11} is hydrogen, fluoro, or hydroxy.

41. (New): A compound or salt according to Claim 39 wherein

A is $H-(Q)_p-$;

Q is independently selected, each time taken, from the group amino acyl;

p is an integer from 1 to 3;

X is O, S, SO, SO_2, or CR^3R^4;

R^3 is fluoro or hydroxy, and R^4 is hydrogen; or R^3 and R^4 together represent =O;

R^{10} is hydrogen or fluoro; and

R^{11} is hydrogen, fluoro, or hydroxy.

42. (New): A compound or salt according to Claim 38 wherein Q is an amino acyl derived from a natural amino acid.

43. (New): A compound or salt according to Claim 39 wherein Q is an amino acyl derived from a natural amino acid.

44. (New): A compound or salt according to Claim 40 wherein Q is an amino acyl derived from a natural amino acid.

45. (New): A compound or salt according to Claim 41 wherein Q is an amino acyl derived from a natural amino acid.

46. (New): A compound or salt according to any one of Claims 38-45 wherein X is SO_2.

47. (New): A compound or salt according to any one of Claims 38-45 wherein X is CR^3R^4, R^3 is fluoro, and R^4 is hydrogen.

48. (New): A compound or salt according to any one of Claims 38-45 wherein X is CR^3R^4, R^3 is hydroxy, and R^4 is hydrogen.

49. (New): A pharmaceutically acceptable salt according to Claim 38 that is an acid-addition salt made with an acid which provides a pharmaceutically acceptable anion; a base-addition salt made with a base which provides a pharmaceutically acceptable anion for a compound which contains an acidic moiety; or a zwitterionic compound which contains oppositely charged groups.

50. (New): A compound according to Claim 38 wherein

A is $H-(Q)_p-$;

Q is L-alanyl;

p is 1;

X is SO_2 or CR^3R^4;

R^3 is fluoro and R^4 is hydrogen;

R^{10} is hydrogen; and

R^{11} is hydrogen;

or the hydrochloride salt, tosylate salt, mesylate salt, esylate salt, besylate salt, or monosodium salt thereof.

51. (New): The pharmaceutically acceptable salt according to Claim 50 which is (1*R*,4*S*,5*S*,6*S*)-4-(2'*S*-Aminopropionyl)amino]-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0.]hexane-4,6-dicarboxylic acid hydrochloride or (1*R*,4*S*,5*S*,6*S*)-4-(2'*S*-2'-Aminopropionyl)amino-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0.]hexane-4,6-dicarboxylic acid tosylate.

52. (New): The compound according to Claim 38 which is (1*R*,4*S*,5*S*,6*S*)-4-(2'S-4'-methylthio-2'-aminobutanonyl)amino-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0]hexane-4,6-dicarboxylic acid or a pharmaceutically acceptable salt thereof.

53. (New): The compound according to Claim 52 which is (1*R*,4*S*,5*S*,6*S*)-4-(2'*S*-4'-methylthio-2'-aminobutanonyl)amino-2,2-dioxo-2λ^6-thia-bicyclo[3.1.0]hexane-4,6-dicarboxylic acid monohydrate.

54. (New): The pharmaceutically acceptable salt according to Claim 38 that is 1*S*,2*S*,4*S*,5*R*,6*R*-2-(2'*S*-aminopropionyl)amino-4-hydroxy-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid hydrochloride.

55. (New): A compound according to Claim 38 wherein

A is H-$(Q)_p$-;

Q is L-alanyl;

p is 1;

X is CR^3R^4;

R^3 is fluoro and R^4 is hydrogen;

R^{10} is hydrogen; and

R^{11} is hydrogen;

or a pharmaceutically acceptable salt thereof.

56. (New): The compound or salt according to Claim 55 which is selected from the group consisting of:

a) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid hydrochloride;

b) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate;

c) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esylate;

d) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid besylate;

e) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid tosylate;

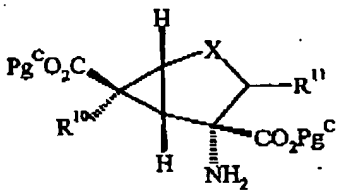
f) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid; and

g) 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic monosodium salt.

57. (New): The pharmaceutically acceptable salt according to Claim 56 which is 1*R*,2*S*,4*R*,5*R*,6*R*-2-(2'*S*-2'-Aminopropionyl)amino-4-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate.

58. (New): The pharmaceutically acceptable salt according to Claim 57 which is (1R,2S,4R,5R,6R)-2-(2'*S*-2'-aminopropionyl)amino-4-fluoro-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid mesylate monohydrate.

59. (New): A process for preparing a compound of Formula I, or a pharmaceutically acceptable salt thereof, as claimed in Claim 38 comprising acylating a compound of formula (ii)



(ii)

with a corresponding amino acyl of Formula III

$$Pg^{N}\text{-}A\text{-} \qquad \text{(III)}$$

wherein Pg^{N} is a nitrogen-protecting group;

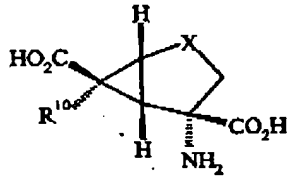
whereafter, for any of the above procedures, when a functional group is protected using a protecting group, removing the protecting group;

whereafter, for any of the above procedures: when a pharmaceutically acceptable salt of a compound of Formula I is required, reacting the basic form of such a compound of Formula I with an acid affording a pharmaceutically acceptable counterion; or for a compound of Formula I which bears an acidic moiety, reacting the acidic form of such a compound of Formula I with a base which affords a pharmaceutically acceptable cation; or for a zwitterionic compound of Formula I, neutralizing the acid-addition salt form or base-addition salt form of such a compound of Formula I; or by any other conventional procedure.

60. (New): A method for affecting the cAMP-linked metabotropic glutamate receptors in a patient, which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 38.

61. (New): A method for affecting the cAMP-linked metabotropic glutamate receptors in a patient, which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 39.

62. (New): A method of administering an effective amount of a compound of Formula II,

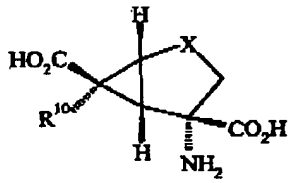


(II)

wherein X and R^{10} are defined as in Claim 38,

which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 38.

63. (New): A method of administering an effective amount of a compound of Formula II,



(II)

wherein X and R^{10} are defined as in Claim 39,

which comprises administering to a patient requiring modulated excitatory amino acid neurotransmission a pharmaceutically effective amount of a compound of Claim 39.

64. (New): A method for treating a neurological disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 38.

65. (New): A method for treating a neurological disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 39.

66. (New): The method of Claim 64 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass and grafting; cerebral ischemia; spinal cord trauma; head trauma; Alzheimer's Disease; Huntington's Chorea; amyotrophic lateral sclerosis; AIDS-induced dementia; perinatal hypoxia; hypoglycemic neuronal damage; ocular damage and retinopathy; cognitive disorders; idiopathic and drug-induced Parkinson's Disease; muscular spasms; migraine headaches; urinary incontinence; drug tolerance, withdrawal, cessation, and craving; smoking cessation; emesis; brain edema; chronic pain; sleep disorders; convulsions; Tourette's syndrome; attention deficit disorder; and tardive dyskinesia.

67. (New): The method of Claim 65 wherein said neurological disorder is cerebral deficits subsequent to cardiac bypass and grafting; cerebral ischemia; spinal cord trauma; head trauma; Alzheimer's Disease; Huntington's Chorea; amyotrophic lateral sclerosis; AIDS-induced dementia; perinatal hypoxia; hypoglycemic neuronal damage; ocular damage and retinopathy; cognitive disorders; idiopathic and drug-induced Parkinson's Disease; muscular spasms; migraine headaches; urinary incontinence; drug tolerance, withdrawal, cessation, and craving; smoking cessation; emesis; brain edema; chronic pain; sleep disorders; convulsions; Tourette's syndrome; attention deficit disorder; and tardive dyskinesia.

68. (New): The method of Claim 66 or 67 wherein said neurological disorder is drug tolerance, withdrawal, cessation, and craving; or smoking cessation.

69. (New): A method for treating a psychiatric disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 38.

70. (New): A method for treating a psychiatric disorder in a patient which comprises administering to the patient in need of treatment thereof a pharmaceutically-effective amount of a compound of Claim 39.

71. (New): The method of claim 69 wherein said psychiatric disorder is schizophrenia, anxiety and related disorders, depression, bipolar disorders, psychosis, and obsessive compulsive disorders.

72. (New): The method of claim 70 wherein said psychiatric disorder is schizophrenia, anxiety and related disorders, depression, bipolar disorders, psychosis, and obsessive compulsive disorders.

73. (New): The method according to any one of Claims 71 or 72 wherein said psychiatric disorder is anxiety and related disorders.

74. (New): A pharmaceutical formulation comprising in association with a pharmaceutically acceptable carrier, dilutent or excipient, a compound of Formula I, or a pharmaceutically acceptable salt thereof.